

This listing of claims will replace all prior versions, and listings, of claims in the application:

**Listing of Claims:**

**1. (Currently Amended)** A method for the treatment of rheumatoid arthritis, comprising administering a compound of formula I



wherein B is a substituted or unsubstituted, up to tricyclic, aryl or heteroaryl moiety of up to 30 carbon atoms with at least one 5- or 6-member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur, wherein if B is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of halogen, up to per-halosubstitution, and  $X_n$ ,

wherein n is 0-3 and each X is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{NO}_2$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$  alkenyl,  $\text{C}_1\text{-C}_{10}$  alkoxy,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_4\text{-C}_{23}$  alkheteroaryl, substituted  $\text{C}_1\text{-C}_{10}$  alkyl, substituted  $\text{C}_2\text{-C}_{10}$  alkenyl, substituted  $\text{C}_1\text{-C}_{10}$  alkoxy, substituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, substituted  $\text{C}_4\text{-C}_{23}$  alkheteroaryl and  $-\text{Y-Ar}$ ;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NO}_2$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$  and halogen up to per-halosubstitution;

wherein  $\text{R}^5$  and  $\text{R}^{5'}$  are independently selected from H,  $\text{C}_1\text{-C}_{10}$  alkyl,  $\text{C}_2\text{-C}_{10}$  alkenyl,  $\text{C}_3\text{-C}_{10}$  cycloalkyl,  $\text{C}_6\text{-C}_{14}$  aryl,  $\text{C}_3\text{-C}_{13}$  heteroaryl,  $\text{C}_7\text{-C}_{24}$  alkaryl,  $\text{C}_4\text{-C}_{23}$  alkheteroaryl, up to per-halosubstituted  $\text{C}_1\text{-C}_{10}$  alkyl, up to per-halosubstituted  $\text{C}_3\text{-C}_{10}$  cycloalkyl, up to per-halosubstituted  $\text{C}_2\text{-C}_{10}$  alkenyl, up to per-halosubstituted  $\text{C}_6\text{-C}_{14}$  aryl and up to per-halosubstituted  $\text{C}_3\text{-C}_{13}$  heteroaryl,

wherein Y is  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{N}(\text{R}^5)-$ ,  $-(\text{CH}_2)_m-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{CH}(\text{OH})-$ ,  $-(\text{CH}_2)_m\text{O}-$ ,  $-(\text{CH}_2)_m\text{S}-$ ,  $-(\text{CH}_2)_m\text{N}(\text{R}^5)-$ ,  $-\text{O}(\text{CH}_2)_m-$ ,  $-\text{CHX}^a$ ,  $-\text{NR}^5\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})-$ ,

$-\text{C}(\text{O})\text{NR}^5-$ ,  $-\text{CX}^a_2-$ ,  $-\text{S}-(\text{CH}_2)_m-$  and  $-\text{N}(\text{R}^5)(\text{CH}_2)_m-$ ,

$m = 1-3$ , and  $\text{X}^a$  is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to perhalosubstitution and optionally substituted by  $\text{Z}_{n1}$ ,

wherein  $n1$  is 0 to 3 and each Z is independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})-\text{NR}^5$ ,  $-\text{NO}_2$ ,  $=\text{O}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{R}^5$ ,  $-\text{SO}_2\text{R}^5$ ,  $-\text{SO}_2\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^5$ ,  $\text{C}_1-\text{C}_{10}$  alkyl,  $\text{C}_1-\text{C}_{10}$  alkoxy,  $\text{C}_3-\text{C}_{10}$  cycloalkyl,  $\text{C}_6-\text{C}_{14}$  aryl,  $\text{C}_3-\text{C}_{13}$  heteroaryl,  $\text{C}_7-\text{C}_{24}$  alkaryl,  $\text{C}_4-\text{C}_{23}$  alkheteroaryl, substituted  $\text{C}_1-\text{C}_{10}$  alkyl, substituted  $\text{C}_3-\text{C}_{10}$  cycloalkyl, substituted  $\text{C}_7-\text{C}_{24}$  alkaryl and substituted  $\text{C}_4-\text{C}_{23}$  alkheteroaryl;

wherein if Z is a substituted group, it is substituted by the one or more substituents independently selected from the group consisting of  $-\text{CN}$ ,  $-\text{CO}_2\text{R}^5$ ,  $-\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{C}(\text{O})\text{NR}^5\text{R}^{5'}$ ,  $=\text{O}$ ,  $-\text{OR}^5$ ,  $-\text{SR}^5$ ,  $-\text{NO}_2$ ,  $-\text{NR}^5\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{R}^{5'}$ ,  $-\text{NR}^5\text{C}(\text{O})\text{OR}^{5'}$ ,  $\text{C}_1-\text{C}_{10}$  alkyl,  $\text{C}_1-\text{C}_{10}$  alkoxy,  $\text{C}_3-\text{C}_{10}$  cycloalkyl,  $\text{C}-\text{C}_{10}$  heteroaryl,  $\text{C}_6-\text{C}_{14}$  aryl,  $\text{C}_4-\text{C}_{24}$  alkheteroaryl and  $\text{C}_7-\text{C}_{24}$  alkaryl

A is a heteroaryl moiety selected from the group consisting of



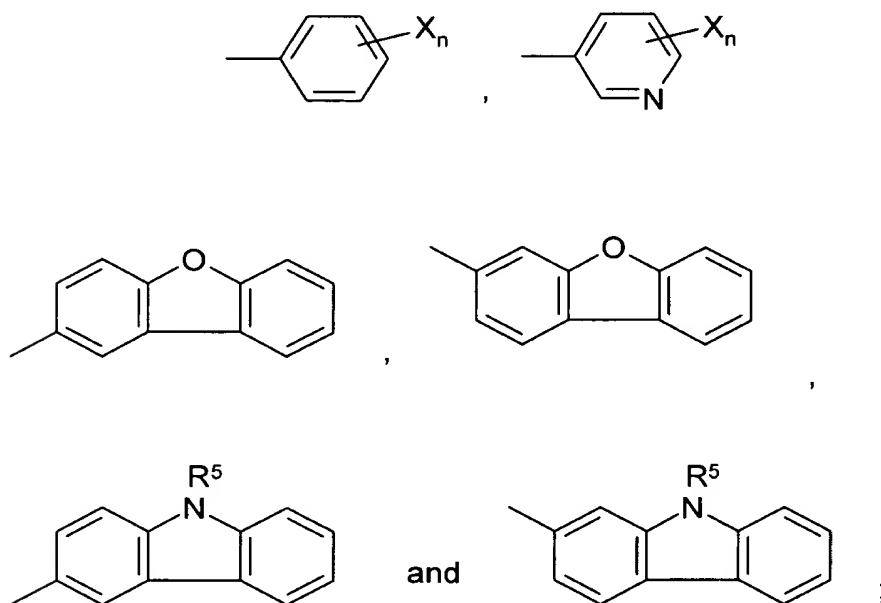
wherein  $R^4$  and  $R^{4'}$  are independently selected from the group consisting of H,  $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_{10}$  cycloalkyl,  $C_6$ - $C_{14}$  aryl,  $C_3$ - $C_{13}$  heteroaryl,  $C_7$ - $C_{24}$  alkaryl,  $C_4$ - $C_{23}$  alkheteroaryl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl, up to per-halosubstituted  $C_3$ - $C_{10}$  cycloalkyl, up to per-halosubstituted  $C_6$ - $C_{14}$  aryl and up to per-halosubstituted  $C_3$ - $C_{13}$  heteroaryl,

$R^a$  is  $C_1$ - $C_{10}$  alkyl,  $C_3$ - $C_{10}$  cycloalkyl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl and up to per-halosubstituted  $C_3$ - $C_{10}$  cycloalkyl; and

$R^b$  is hydrogen or halogen,

$R^e$  is hydrogen, halogen,  $C_1$ - $C_{10}$  alkyl, up to per-halosubstituted  $C_1$ - $C_{10}$  alkyl or combines with  $R^1$  and the ring carbon atoms to which  $R^1$  and  $R^e$  are bound to form a 5- or 6-membered cycloalkyl, aryl or heteraryl ring with 0-2 members selected from O, N and S.

**2. (Original)** A method as in claim 1, wherein B is up to a tricyclic aromatic ring structure selected from the group consisting of



which is substituted or unsubstituted by halogen, up to per-halosubstitution, and

wherein  $n = 0-3$  and each X is independently selected from the group consisting of  $-CN$ ,  $-CO_2R^5$ ,  $-C(O)NR^5R^{5'}$ ,  $-C(O)R^5$ ,  $-NO_2$ ,  $-OR^5$ ,  $-SR^5$ ,  $-NR^5R^{5'}$ ,  $-NR^5C(O)OR^{5'}$ ,  $-NR^5C(O)R^{5'}$ ,  $C_1$ - $C_{10}$  alkyl,  $C_{2-10}$ -alkenyl,  $C_{1-10}$ -alkoxy,  $C_3$ - $C_{10}$  cycloalkyl,  $C_6$ - $C_{14}$

aryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, and substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>2-10</sub>-alkenyl, substituted C<sub>1-10</sub>-alkoxy, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl and -Y-Ar;

wherein if X is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, NO<sub>2</sub>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup> and halogen up to per-halosubstitution;

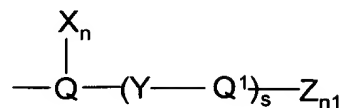
wherein R<sup>5</sup> and R<sup>5'</sup> are independently selected from H, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>2-10</sub>-alkenyl, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>2-10</sub>-alkenyl, up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>6</sub>-C<sub>14</sub> aryl and up to per-halosubstituted C<sub>3</sub>-C<sub>13</sub> heteroaryl,

wherein Y is -O-, -S-, -N(R<sup>5</sup>)-, -(CH<sub>2</sub>)<sub>m</sub>-, -C(O)-, -CH(OH)-, -(CH<sub>2</sub>)<sub>m</sub>O-, -NR<sup>5</sup>C(O)NR<sup>5</sup>R<sup>5'</sup>-, -NR<sup>5</sup>C(O)-, -C(O)NR<sup>5</sup>-, -(CH<sub>2</sub>)<sub>m</sub>S-, -(CH<sub>2</sub>)<sub>m</sub>N(R<sup>5</sup>)-, -O(CH<sub>2</sub>)<sub>m</sub>-, -CHX<sup>a</sup>, -CX<sup>a</sup><sub>2</sub>-, -S-(CH<sub>2</sub>)<sub>m</sub>- and -N(R<sup>5</sup>)(CH<sub>2</sub>)<sub>m</sub>-,

m = 1-3, and X<sup>a</sup> is halogen; and

Ar is a 5-10 member aromatic structure containing 0-4 members of the group consisting of nitrogen, oxygen and sulfur which is unsubstituted or substituted by halogen up to per-halo and optionally substituted by Z<sub>n1</sub>, wherein n1 is 0 to 3 and each Z is independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)R<sup>5</sup>, =O, -SO<sub>2</sub>R<sup>5</sup>, -SO<sub>2</sub>NR<sup>5</sup>R<sup>5'</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, -C(O)R<sup>5</sup>, -NO<sub>2</sub>, -OR<sup>5</sup>, -SR<sup>5</sup>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>3</sub>-C<sub>13</sub> heteroaryl, C<sub>7</sub>-C<sub>24</sub> alkaryl, C<sub>4</sub>-C<sub>23</sub> alkheteroaryl, substituted C<sub>1</sub>-C<sub>10</sub> alkyl, substituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, substituted C<sub>7</sub>-C<sub>24</sub> alkaryl and substituted C<sub>4</sub>-C<sub>23</sub> alkheteroaryl; wherein if Z is a substituted group, it is substituted by one or more substituents independently selected from the group consisting of -CN, -CO<sub>2</sub>R<sup>5</sup>, -C(O)NR<sup>5</sup>R<sup>5'</sup>, =O, -OR<sup>5</sup>, -SR<sup>5</sup>, -NO<sub>2</sub>, -NR<sup>5</sup>R<sup>5'</sup>, -NR<sup>5</sup>C(O)R<sup>5'</sup>, -NR<sup>5</sup>C(O)OR<sup>5'</sup>, C<sub>1</sub>-C<sub>10</sub> alkyl, C<sub>1</sub>-C<sub>10</sub> alkoxy, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C-C<sub>10</sub> heteroaryl, C<sub>6</sub>-C<sub>14</sub> aryl, C<sub>4</sub>-C<sub>24</sub> alkheteroaryl and C<sub>7</sub>-C<sub>24</sub> alkaryl.

**3. (Previously Presented)** A method of claim 1, wherein B is



wherein Y is selected from the group consisting of -O-, -S-, -CH<sub>2</sub>-, -SCH<sub>2</sub>-, -CH<sub>2</sub>S-, -CH(OH)-, -C(O)-, -CX<sup>a</sup><sub>2</sub>, -CX<sup>a</sup>H-, -CH<sub>2</sub>O- and -OCH<sub>2</sub>-, where X<sup>a</sup> is halogen,

Q is a six member aromatic structure containing 0-2 nitrogen, substituted or unsubstituted by halogen, up to per-halosubstitution;

Q<sup>1</sup> is a mono- or bicyclic aromatic structure of 3 to 10 carbon atoms and 0-4 members of the group consisting of N, O and S, unsubstituted or unsubstituted by halogen up to per-halosubstitution, and

X, Z, n and n1 are as defined in claim 1 and s is 0 or 1.

**4. (Original)** A method as in claim 3, wherein

Q is phenyl or pyridinyl, substituted or unsubstituted by halogen, up to per-halosubstitution,

Q<sup>1</sup> is selected from the group consisting of phenyl, pyridinyl, naphthyl, pyrimidinyl, quinoline, isoquinoline, imidazole and benzothiazolyl, substituted or unsubstituted by halogen, up to per-halo substitution, or -Y-Q<sup>1</sup> is phthalimidinyl substituted or unsubstituted by halogen up to per-halo substitution, and

Z and X are independently selected from the group consisting of -R<sup>6</sup>, -OR<sup>6</sup> and -NHR<sup>7</sup>, wherein R<sup>6</sup> is hydrogen, C<sub>1</sub>-C<sub>10</sub>-alkyl or C<sub>3</sub>-C<sub>10</sub>-cycloalkyl and R<sup>7</sup> is selected from the group consisting of hydrogen, C<sub>3</sub>-C<sub>10</sub>-alkyl, C<sub>3</sub>-C<sub>6</sub>-cycloalkyl and C<sub>6</sub>-C<sub>10</sub>-aryl, wherein R<sup>6</sup> and R<sup>7</sup> can be substituted by halogen or up to per-halosubstitution.

**5. (cancelled)**

**6. (cancelled)**

**7. (cancelled)**

**8. (currently amended)** A method as in claim 15, wherein R<sup>1</sup> is t-butyl.

**9. (cancelled)**

**10. (cancelled)**

11. (cancelled)
12. (cancelled)
13. (cancelled)
14. (cancelled)
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24. (cancelled)
25. (cancelled)
26. (cancelled)
27. (cancelled)

28. (original) A method as in claim 1, wherein the compound for formula I displays p38 IC<sub>50</sub>'s of less than 10  $\mu$ m as determined by an in-vitro p38 kinase inhibition assay.

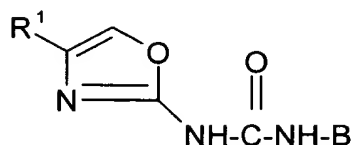
29. (cancelled)

30. (Original) A method according to claim 1, comprising administering an amount of a compound of formula I effective to inhibit p38.

31. (cancelled )
32. (cancelled)
33. (cancelled)
34. (cancelled)
35. (cancelled)
36. (cancelled)

37. (cancelled)

38. (Currently amended) A method as in claim 1 comprising administering a compound of the formula



wherein R<sup>1</sup> is t-butyl and B are as defined in claim 1.

39. (cancelled)

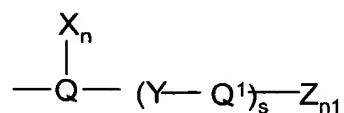
40. (cancelled)

41. (cancelled)

42. (cancelled)

43. (cancelled)

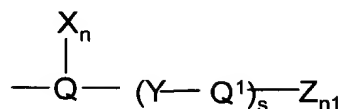
44. (Currently amended) A method as in claim 1 5, wherein B is of the formula



wherein Q is phenyl or pyridinyl, optionally substituted by halogen up to per-halosubstitution, Q<sup>1</sup> is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -CH<sub>2</sub>S-, -SCH<sub>2</sub>-, -CH<sub>2</sub>O-, -OCH<sub>2</sub>- or -CH<sub>2</sub>-, X is C<sub>1</sub>-C<sub>4</sub> alkyl or up to per-halosubstituted C<sub>1</sub>-C<sub>4</sub> alkyl and Z is as defined in claim 1, n = 0 or 1, s = 1 and n1 = 0-1.



**45. (currently amended)** A method as in claim 38 9, wherein B is of the formula



Q is phenyl or pyridinyl, optionally substituted by halogen up to per-halosubstitution, Q<sup>1</sup> is pyridinyl, phenyl or benzothiazolyl optionally substituted by halogen up to per-halosubstitution, Y is -O-, -S-, -C(O)- or -CH<sub>2</sub>-, X is C<sub>1</sub>-C<sub>4</sub> alkyl or up to per-halosubstituted C<sub>1</sub>-C<sub>4</sub> alkyl and Z is as defined in claim 1 n = 0 or 1, s = 0 or 1 and n<sub>1</sub> = 0 or 1.

**46. (cancelled)**

**47. (cancelled)**

**48. (cancelled)**

**49. (cancelled)**

**50. (Previously Presented)** A method as in claim 1, wherein B is

a) phenyl, pyridinyl, naphthyl, quinolinyl or isoquinolinyl, substituted by -Y-Ar and optionally substituted by

- halogen up to per-halosubstitution,
- C<sub>1</sub>-C<sub>4</sub> alkyl,
- up to per-halosubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, or
- a combination thereof,

wherein Y and Ar are as defined in claim 1;

- b) thienyl substituted by methyl; or
- c) indolyl substituted by phenyl or pyridyl.

**51. (Previously Presented)** A method as in claim 1, wherein B is phenyl or pyridinyl substituted by -Y-Ar and optionally substituted by

- halogen ,up to per-halosubstitution,
- C<sub>1</sub>-C<sub>4</sub> alkyl,
- up to per-halosubstituted C<sub>1</sub>-C<sub>4</sub> alkyl, or

- a combination thereof,

wherein Y and Ar are as defined in claim 1.

**52. (cancelled)**

**53. (Withdrawn currently amended )** A pharmaceutical composition comprising a compound according to claim ~~52~~ 1 or a pharmaceutically acceptable salt thereof and a physiologically acceptable carrier.

**54. (cancelled)**

**55. (Previously Presented)** A method according to claim 1, wherein R<sup>1</sup> is selected from the group consisting of halogen, C<sub>3</sub>-C<sub>10</sub> cycloalkyl, C<sub>1</sub>-C<sub>13</sub> heteroaryl, C<sub>6-14</sub> aryl, C<sub>7-24</sub> alkaryl, up to per-halosubstituted C<sub>1</sub>-C<sub>10</sub> alkyl, up to per-halosubstituted C<sub>3</sub>-C<sub>10</sub> cycloalkyl, up to per-halosubstituted C<sub>1</sub>-C<sub>13</sub> heteroaryl, up to per-halosubstituted C<sub>6-14</sub> aryl, and up to per-halosubstituted C<sub>7-24</sub> alkaryl.

**56. (cancelled)**

**57. (cancelled)**

**58. (Previously Presented)** A method for the treatment of rheumatoid arthritis comprising administering to a patient in need thereof a pharmaceutically effective amount of a compound of formula

